

Can I treat this pregnant patient with botulinum toxin?

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Abstract

Botulinum toxin type A (BoNT-A) is used extensively in the neurological setting, most commonly for the management of dystonia and spasticity. It is inevitable that female patients who derive a significant benefit from botulinum toxin treatment may inadvertently be injected in as-yet undiagnosed pregnancy or may be planning to become pregnant. Following an examination of the evidence for the safety of botulinum toxin in pregnancy, physicians and patients should be reassured as to the absence of evidence of harm in case reports of botulism and accidental or intentional botulinum toxin injection and the improbability of crossing the placenta. Consequently, judgment should be made that acknowledges that when botulinum toxin treatment is to continue through pregnancy it should be because this will represent the lesser harm in view of the severity of the mother's symptoms and the physical and psychological harm caused by withholding treatment. It is also normally appropriate to reassure patients inadvertently injected.

INTRODUCTION

Botulinum toxin type A (BoNT-A) is used in the treatment of dystonia. The commonest form, cervical dystonia, is more frequent in women and many are still of child bearing age[1]; it is inevitable that patients on botulinum toxin treatment will from time to time either be planning to become pregnant or may wish to be treated while pregnant. In addition to cervical dystonia, the newer indication of BoNT-A for chronic migraine – a female predominant disorder – will make this an increasingly common issue,[2] not to mention the use of BoNT-A in a wider cosmetic setting. To help the patient make an informed choice we need to determine what is known of the risks of botulinum toxin treatment in pregnancy and lactation.

There are two relevant situations. Firstly, the risks arising from an injection of BoNT-A in a patient who is unaware they are pregnant, and secondly the risks of continuing or curtailing treatment in an already pregnant patient.

The international regulatory bodies are not proscriptive. The Medicines and Healthcare products Regulatory Agency (MHRA) recommend that caution is exercised when prescribing BoNT-A.[3] All BoNT-A preparations are Food and Drug Administration (FDA) category C, which means that there have been inadequate studies on the use of BoNT-A in pregnant women,[4] but that studies in animals have shown there to be an adverse effect on the foetus.[5,6] Molecules less than 500Da have incomplete transfer across

the placenta; botulinum toxin is a large molecule (150kDa) and therefore unlikely to cross the placenta by passive diffusion.[7] Active transport across the placenta cannot be excluded.

Despite the caution, there is no definitive evidence that treatment with BoNT-A during pregnancy carries a risk. There are a growing number of reports of the outcome of pregnancy following botulism [8,9] or after therapeutic injection that have not been attended by evidence of foetal harm.[10-18] Long term follow up of the resulting child is usually lacking. There is no evidence of harm – but absence of evidence is not evidence of absence.

Dystonia seriously undermines self-confidence and produces pain, deformity and loss of function. It is known that dystonia has an impact on quality of life greater than that seen in conditions considered more serious, such as multiple sclerosis and Parkinson's disease.[19] For those patients who respond to treatment of migraine, BoNT-A can be life transforming and the prospect of cessation of treatment may be daunting for the patient. In making a judgment, the impact of the untreated disorder must be considered by both neurologists and patients.

There is thus insufficient evidence to allow truly informed consent. Despite this however, in a survey of physicians using BoNT-A, of the respondents that had injected BoNT-A during pregnancy, half reported that they felt either “somewhat” or “very comfortable” injecting during pregnancy.[20]

The epilepsy pregnancy registries [21,22] provide an excellent model that has provided invaluable insights into the relative risks of different anticonvulsants. A similar botulinum toxin in pregnancy register could relatively readily provide the evidence that is needed to allow women considering pregnancy, or inadvertently exposed to botulinum toxin during pregnancy, to be as fully informed to make decisions on their continued treatment.

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